IN THE CLAIMS

Please cancel claims 63, 71, 75, 79, 81, 89, 90, 94, and 102, without prejudice.

Please enter the following amended claims:

71 66. (Amended) The method of claim 139, wherein said GPCR is a taste receptor.

72 67. (Twice Amended) The method of claim 139, wherein said reporter gene is selected from the group consisting of luciferase, GFP, chloramphenicol acetyl transferase, β-galactosidase, β-lactamase and secreted alkaline phosphatase.

73 68. (Amended) The method of claim 139, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

74 74. (Amended) The method of claim 140, wherein said signal transduction detection system comprises an intracellular calcium indicator.

75 78. (Amended) The method of claim 141, wherein said signal transduction detection system comprises an intracellular calcium indicator.

76 80. (Amended) The method of claim 141, wherein said detecting comprises fluorescence detection.

77 84. (Amended) The method of claim 142, wherein said detecting comprises fluorescence detection.

78 85. (Amended) The method of claim 142, wherein said reporter gene is selected from the group consisting of luciferase, GFP, chloramphenicol acetyl transferase, β-galactosidase, β-lactamase and secreted alkaline phosphatase.

J9 86. (Amended) The method of claim 142, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

J10 93. (Amended) The method of claim 143, wherein said signal transduction detection system comprises an intracellular calcium indicator.

J11 97. (Amended) The method of claim 144, wherein said detecting comprises fluorescence detection.

J12 98. (Twice amended) The method of claim 144, wherein said reporter gene is selected from the group consisting of luciferase, GFP, chloramphenicol acetyl transferase, β-galactosidase, β-lactamase and secreted alkaline phosphatase.

J13 99. (Amended) The method of claim 144, further comprising contacting said cell with a compound that increases calcium levels inside said cell.

J14 105. (Amended) The method of claim 145, wherein said detecting comprises fluorescence detection.

J15 106. (Twice amended) The method of claim 145, wherein said reporter gene is selected from the group consisting of luciferase, GFP, chloramphenicol acetyl transferase, β-galactosidase, β-lactamase and secreted alkaline phosphatase.

J16 107. (Amended) The method of claim 145, further comprising contacting said cells with a compound that increases calcium levels inside said cells.

J17 122. (Twice amended) The method of claim 141, wherein said GPCR is selected from the group consisting of muscarinic receptors, nicotinic acetylcholine receptors, GABA receptors, glutamate receptors, adrenergic receptors, dopamine receptors and serotonin receptors.

f17 123. (Twice amended) The method of claim 142, wherein said GPCR is selected from the group consisting of muscarinic receptors, nicotinic acetylcholine receptors, GABA receptors, glutamate receptors, adrenergic receptors, dopamine receptors and serotonin receptors

124. (Amended) The method of claim 143, wherein said GPCR is selected from the group consisting of muscarinic receptors, nicotinic acetylcholine receptors, GABA receptors,

f18 glutamate receptors, adrenergic receptors, dopamine receptors and serotonin receptors.

125. (Amended) The method of claim 144, wherein said GPCR is selected from the group consisting of muscarinic receptors, nicotinic acetylcholine receptors, GABA receptors, glutamate receptors, adrenergic receptors, dopamine receptors and serotonin receptors.

129. (Amended) The method of claim 139, wherein said second heterologous promoter is NFAT.

130. (Amended) The method of claim 142, wherein said second heterologous promoter is NFAT.

f19

131. (Amended) The method of claim 144, wherein said second heterologous promoter is NFAT.

132. (Amended) The method of claim 145, wherein said second heterologous promoter is NFAT.

f20 133. (Twice amended) The method of claim 139, wherein said method further comprises comparing said change in reporter gene expression detected in step (iii) with a change in reporter gene expression detected in a control cell line lacking said GPCR detected under the same conditions as in step (iii), wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a

cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

134. (Twice amended) The method of claim 140, wherein said method further comprises comparing said change in signal detected in step (iii) with a change in signal detected in a control cell line lacking said GPCR detected under the same conditions as in step (iii) , wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

135. (Twice amended) The method of claim 141, wherein said method further comprises comparing said change in signal detected in step (ii) with a change in signal detected in a control cell line lacking said GPCR detected under the same conditions as in step (ii), wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

g 20 Cont

136. (Twice amended) The method of claim 142, wherein said method further comprises comparing said change in reporter gene expression detected in step (ii) with a change in reporter gene expression detected in a control cell line lacking said GPCR detected under the same conditions as in step (ii), wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and

wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

137. (Twice Amended) The method of claim 143, wherein said method further comprises comparing said change in reporter gene expression detected in step (iii) with a change in signal detected in a control cell line lacking said GPCR wherein said change is detected under the same conditions as in steps (ii) and (iii), wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

J20

138. (Twice amended) The method of claim 144, wherein said method further comprises comparing said change in reporter gene expression detected in step (iii) with a change in reporter gene expression detected in a control cell line lacking said GPCR, detected under the same conditions as in step (ii) and (iii), wherein the control cell line is a COS-7 cell line comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

139. (Amended) A method of identifying a G-protein coupled receptor (GPCR) for a given ligand, the method comprising:

(i) providing a cell, said cell comprising,

J21

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2,

b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene, and

c) a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction,

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein,

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is not naturally expressed in said cell,

wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system;

(ii) contacting said cell with said ligand; and

(iii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said ligand with reporter gene expression after addition of said ligand, wherein the cell is a COS-7 cell comprising polynucleotides according to a, b, and c, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

140. (Amended) A method for identifying a G-protein coupled receptor (GPCR) for a given ligand, the method comprising:

(i) providing a cell, said cell comprising,

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2, and

b) a second heterologous promoter operably linked to a second polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction, and

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein, and

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is normally coupled to either $G\alpha_i$, $G\alpha_s$ or $G\alpha_{12}$ in the absence of said Gα15 protein,

wherein said GPCR is not naturally expressed in said cell, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system;

321 Cont

(ii) contacting said cell with said ligand; and

(iii) detecting a change in a signal with a signal transduction detection system by comparing said signal prior to addition of said ligand with said signal after addition of said ligand, wherein said signal transduction detection system comprises a dye, wherein the cell is a COS-7 cell comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further

comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

141. (Amended) A method of a identifying a ligand for a G-protein coupled receptor (GPCR), the method comprising:

(i) contacting a cell with a test chemical, said cell comprising

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2, and

b) a second heterologous promoter operably linked to a second polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction,

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein,

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is normally coupled to either $G\alpha_i$, $G\alpha_s$ or $G\alpha_{12}$ in the absence of said Gα15 protein,

wherein said GPCR is not naturally expressed in said cell, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system; and

(ii) detecting a change in a signal with a signal transduction detection system

by comparing said signal prior to addition of said test chemical with said signal after addition of said test chemical, wherein said signal transduction detection system

121 cont

comprises a dye, wherein a change in reporter gene expression identifies the test compound as a ligand for the GPCR, thereby identifying the ligand for the GPCR, wherein the cell is a COS-7 cell comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

142. (Amended) A method of identifying a ligand for a G-protein coupled receptor (GPCR), the method comprising

(i) contacting a cell with a test chemical, said cell comprising,

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2,

b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene, and

c) a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction, and

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein, and

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is not naturally expressed in said cell, and

121 cont

wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system; and

(ii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said test chemical with reporter gene expression after addition of said test chemical, wherein a change in reporter gene expression identifies the test compound as a ligand for the GPCR, thereby identifying the ligand for the GPCR, wherein the cell is a COS-7 cell comprising polynucleotides according to a, b, and c, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

121 cont

143. (Amended) A method for identifying a modulator of signal transduction mediated by G-protein coupled receptor (GPCR) activation in a cell, the method comprising:

(i) contacting a cell with a ligand that in the absence of a test chemical, activates signal transduction in said cell, said cell comprising

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2, and

b) a second heterologous promoter operably linked to a second polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction, and

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein, and

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is normally coupled to either $G\alpha_i$, $G\alpha_s$ or $G\alpha_{12}$ in the absence of said Gα15 protein,

wherein said GPCR is not naturally expressed in said cell, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system;

(ii) contacting said cell with the test compound, and

(iii) detecting a change in a signal with a signal transduction detection system by comparing said signal prior to addition of said test chemical with said signal after addition of said test chemical, wherein the cell is a COS-7 cell comprising polynucleotides according to a and b, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

121 Cont

144. (Amended) A method for identifying a modulator of signal transduction in a cell, the method comprising:

(i) contacting a cell with a ligand that in the absence of a test chemical, activates signal transduction via a GPCR in said cell, said cell comprising,

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2,

b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene, and

c) a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction,

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein,

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said GPCR is not naturally expressed in said cell,

wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein, and

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system;

(ii) contacting said cell with the test compound; and

(iii) detecting a change in reporter gene expression by comparing reporter gene expression prior to addition of said test chemical with reporter gene expression after addition of said test chemical, wherein the cell is a COS-7 cell comprising polynucleotides according to a, b, and c, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.

g21 cont

145. (Amended) A method of functionally profiling a test chemical, comprising the steps of:

(i) contacting a panel of cells with a test chemical, said panel of cells comprising a plurality of cell clones, each cell clone comprising

a) a first heterologous inducible promoter operably linked to a first polynucleotide encoding a functional Gα15 protein having at least 95% sequence homology to SEQ. ID. NO. 2,

b) a second heterologous promoter operably linked to a second polynucleotide encoding a reporter gene, and

c) a third heterologous promoter operably linked to a third polynucleotide encoding said GPCR,

wherein said first heterologous inducible promoter provides for the low level expression prior to induction,

wherein induction of said first heterologous inducible promoter provides for at least a three fold increase in expression of said Gα15 protein,

wherein induced expression of said Gα15 protein is sufficient to permit promiscuous coupling to said GPCR,

wherein said second heterologous promoter is directly or indirectly modulated by the activity of said Gα15 protein,

wherein said GPCR is not naturally expressed in said cell,

wherein said cell arises from a cell line subjected to functional cell analysis with a signal transduction detection system; and

wherein each cell clone differs only with respect to said GPCR that is expressed;

145 cont

(ii) contacting said cell clones with a test chemical;

(iii) detecting reporter gene expression from said cell clones; and

(iv) comparing reporter gene expression between said cell clones, wherein the cell is a COS-7 cell comprising polynucleotides according to a, b, and c, wherein the first heterologous inducible promoter is a cytomegalovirus (CMV) promoter operably linked to a heptamerized tet operator, and wherein the cells further comprise a polynucleotide encoding a tetracycline-dependent transactivator operably linked to a constitutive promoter.